Renal Artery Embolization: Application and Success in Patients with Renal Cell Carcinoma and Angiomyolipoma

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ABSTRACT

Renal artery embolization is a procedure primarily performed by interventional radiologists that can be utilized for treatment of renal tumors, both malignant and benign. It has many applications, including pretreatment of renal cell carcinomas prior to planned resection to decrease hemorrhagic complications intraoperatively, treatment of malignant renal tumor in patients who are not deemed suitable surgical candidates, as well as treatment of benign renal tumors and their potential hemorrhagic complications. There are many different techniques. We describe how the procedure is approached at the University of Florida–Gainesville and provide examples of two cases, a renal cell carcinoma and an angiomyolipoma, treated at our institution with transcatheter embolotherapy.

KEYWORDS: Renal artery embolization, renal cell carcinoma, angiomyolipoma

Objectives: Upon completion of this article, the reader should understand the indications and technique used in embolization of renal masses, including long-term follow-up.
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Renal artery embolization is a technique by which arterial blood flow can either be decreased or completely terminated to prepare a patient with a renal neoplasm more safely for surgical resection (as in the case of renal cell carcinoma) or even treat and prevent life-threatening hemorrhage therapeutically (as in the case of angiomyolipoma).

Renal cell carcinoma (RCC) is the most common malignant neoplasm of the kidney. This tumor is largely composed of clear cells, often encapsulated, and usually very vascular.[1] It is known to grow into the renal pelvis and subsequently into the renal vein and inferior vena cava, which does not preclude surgical resection. It is also known to be associated with von Hippel-Lindau syndrome (VHL), particularly when tumor is found in multiple locations or bilaterally.

Indications for treatment of RCC with transcatheter embolotherapy include preoperative devascularization to ease resection and decrease blood loss, palliative therapy in patients with unresectable tumor or who are not surgical candidates, and treatment of hemorrhagic complications, including spontaneous

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Case-Based Interventional Radiology; Guest Editors , Ron C. Gaba, M.D., Derek L. West, M.D., James T. Bui, M.D., Charles A. Owens, M.D.
Semin Intervent Radiol 2007;24:111–116.
DOI 10.1055/s-2007-971185. ISSN 0739-9529.

rupture of previously undiagnosed tumor.[1,2] Additionally, some evidence suggests that preoperative embolization of RCC is associated with improved mortality rates when compared with surgical treatment alone.[3]

Ultrasound (US) of RCC typically demonstrates a circumscribed renal lesion with variable echogenicity. Smaller lesions are more likely to demonstrate hyperechogenicity and may be mistaken for an angiomyolipoma (AML).[4] Contrast-enhanced computed tomography (CT), with images obtained both prior to and following contrast administration, typically demonstrate a solid circumscribed lesion that demonstrates enhancement. Less common characteristics of RCC include those with more cystic features. Sensitivity for detection of renal lesions is most pronounced in the nephrographic phase of contrast enhancement, whereas sensitivity for venous invasion is most pronounced in the corticomedullary phase of enhancement.[5] Presumptive diagnosis of RCC can often be made with enhancement >10 Hounsfield units (HU) when comparing pre- and postcontrasted images;[6] however many RCC enhance greater than 20 HU.[7]

Arterial phase imaging during diagnostic CT, with imaging commencing 20 to 25 seconds following contrast administration (at least 4 mL/s injection), can help identify renal arterial anatomy with regard to the renal tumor, thus providing a roadmap prior to transcatheter therapy. Similarly, angiographic evaluation may demonstrate a constellation of findings. These include neovascularity, hypervascularity, dilation of the main renal artery, tumor stain, contrast pooling, displacement of normal renal vessels, as well as arteriovenous shunts with early venous drainage.[1]

Magnetic resonance (MR) evaluation of renal lesions is similar to that of contrast CT. Gadolinium contrast is utilized and images are obtained. RCC tumors are typically isointense to hypointense on T1-weighted images, and they demonstrate contrast enhancement.

AML, however, is a benign tumor classified as a renal hamartoma, and it is made up of blood vessels, smooth muscle cells, lipid, and connective tissues.[8] AMLs are usually solitary. However, they may be multiple in ~20% of cases, particularly when associated with tuberous sclerosis (TS).[9] The main complicating feature of AML is related to hemorrhage, which can become quickly life threatening. The propensity for hemorrhage is thought to be multifactorial and related to deficiencies of elastic tissue, hypervascularity, venous invasion, and predisposition for development of focal pseudoaneurysms within the arterial vessels of the tumor.[9]

Indications for treatment of AML with transcatheter embolotherapy include those which present with hemorrhage and hemodynamic instability, as well as those which are found to be >4 cm. The natural history of AML is that those lesions <4 cm are likely to remain asymptomatic and are at low risk for hemorrhagic complications.[10] These smaller lesions may be followed conservatively, primarily with CT.

US of angiomyolipomas typically shows an echogenic circumscribed renal mass that is often round or oval and cortical in location. There may be acoustical shadowing behind the lesion. CT imaging demonstrates a lesion with various regions of fat density. HU measurements of <-20 are widely accepted as diagnostic of intralesional fat and therefore diagnostic of AML. One must be aware, however, of AML with minimal fat content, which may present with spontaneous hemorrhage without identifiable intralesional fat.[11]

MR imaging of AML often shows a circumscribed mass with fat density (high on T1- and T2-weighted images). One must be sure, however, not to assume fat content within a renal lesion when identifying high T1 signal because blood products and proteinaceous fluid can both demonstrate high T1 signal and mimic fat. Because of the lack of specificity with standard MR imaging, fat suppression techniques are often used. Chemical shift techniques, however, which are excellent at identifying microscopic fat (as in adrenal adenomas), are not as good at identifying the macroscopic fat associated with renal AML.[12]

On angiographic evaluation, AML are hypervascular in 95% of cases. The arteries within the tumor are often tortuous, irregular, and, classically, aneurysmal (related to pseudoaneurysm formation in the tumor vessels). Venous pooling exists, often with a sunburst whorled appearance, without the presence of arteriovenous shunting. Absence of shunting and the presence of pseudoaneurysms help distinguish AML from RCC on angiogram.[13]

EMBOLIZATION TECHNIQUE

The right common femoral artery (CFA) approach is commonly used for percutaneous renal intervention. At our institution, access is gained via a 22-gauge micropuncture system, 3/4F coaxial catheter, and a 0.035 Bentson wire (Cook, Bloomington, IN). A short 5F sheath is then placed and secured to the skin, and a 5F flush catheter advanced to the level of T11. An aortogram is performed to evaluate accessory renal arteries or possible parasitized vessels. In ~25% of cases there is a renal accessory artery, which is usually inferior to the main and supplies the inferior pole (Fig. 1A).[1,14] The renal arteries usually arise at the L1-L2 level and can be accessed with a 4F Cobra 2, SOS 0, or Hook catheter (AngioDynamics, Queensbury, NY). A subtraction run at 5 to 6 mL/s is sufficient to opacify the renal vessels with standard nonionic contrast. At least two projections are obtained to fully evaluate the entire vascular tree. CO_2 angiography is recommended for patients with chronic renal insufficiency because gadolinium may cause nephrotoxicity at levels needed for

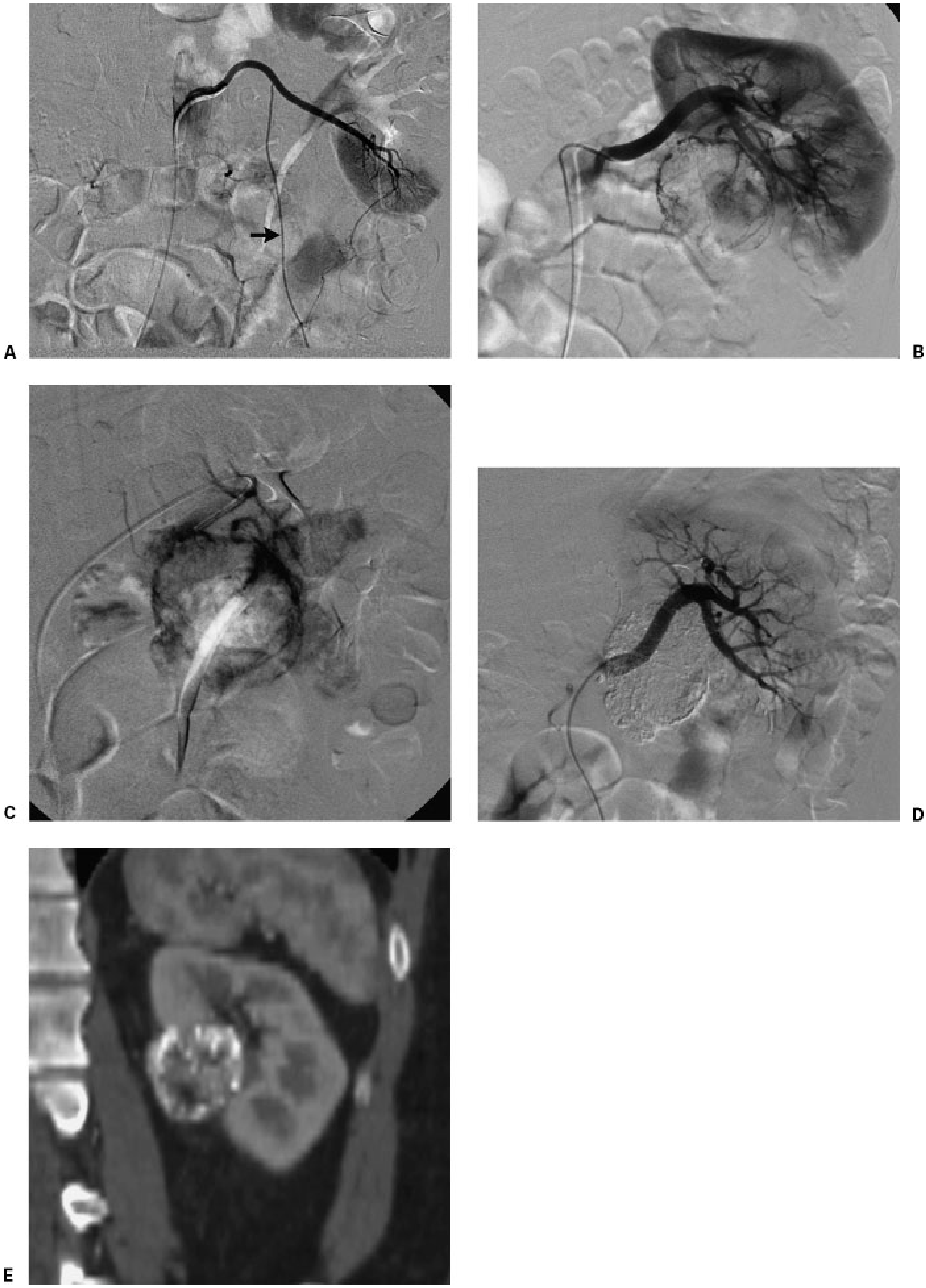

Figure 1 (A) Subtraction arteriogram of left inferior accessory renal artery feeding inferior pole. Note left gonadal artery (arrow) arising from proximal accessory renal and lack of tumor blush. (B) Subtraction arteriography demonstrates large medial hypervascular mass correlating to known angiomyolipoma (AML) with single feeding vessel. (C) Subtraction images during subselective catheterization of feeding vessel to AML with SOS 0 Selective Catheter (AngioDynamics, Queensbury, NY). (D) Subtraction arteriography postembolization with 1:1 Ethiodol and ethanol. (E) Contrast-enhanced CT 5 weeks postembolization of left kidney shows residual Ethiodol in mass without infarction of adjacent renal parenchyma.

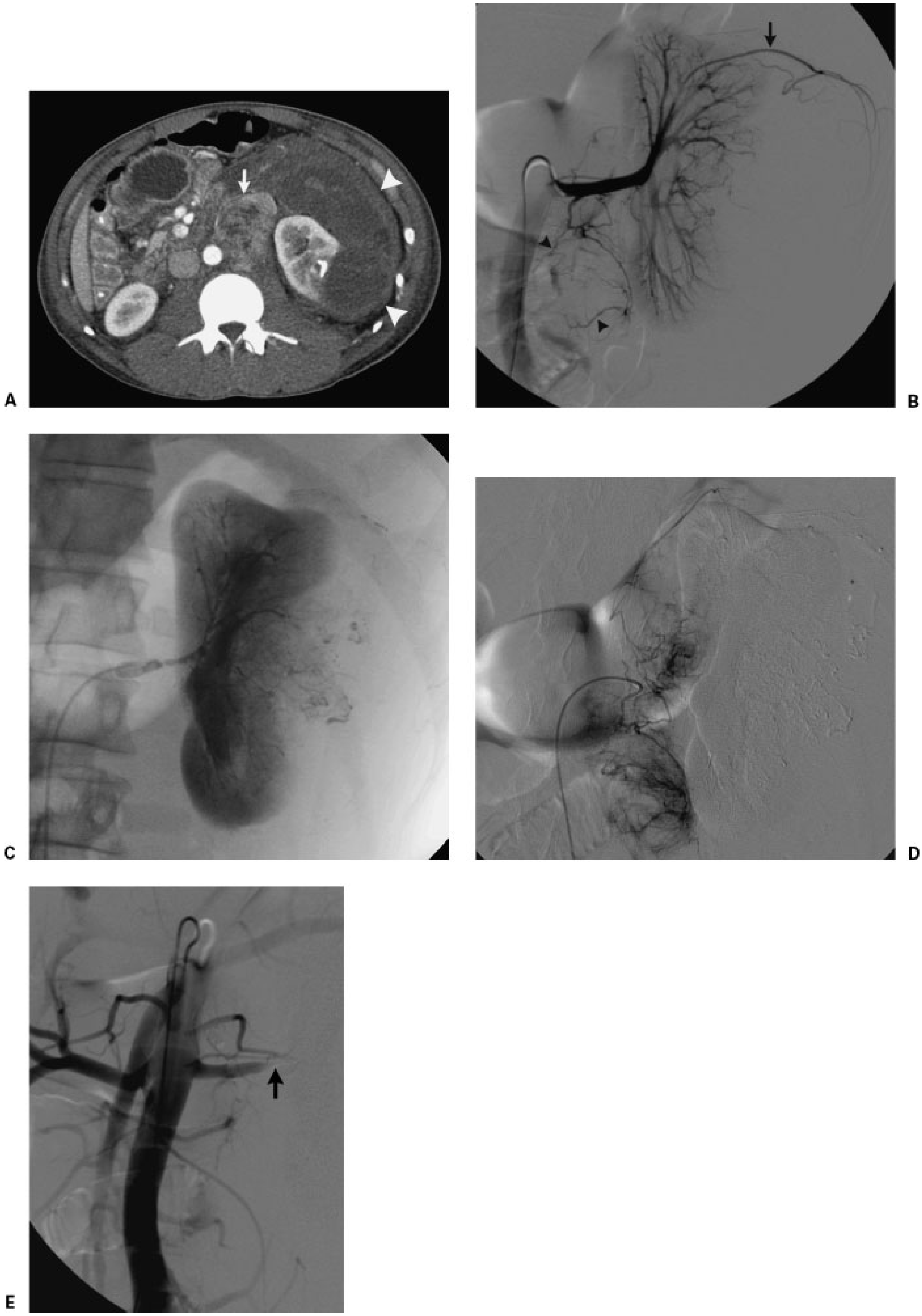

Figure 2 (A) Contrast-enhanced computed tomography (CT) of previously healthy patient demonstrates large hemorrhagic lesion (arrowhead) arising from left kidney with large hypervascular periaortic lymph nodes (arrow). (B) Selective subtraction renal angiography demonstrates lateral mass compressing kidney medially with superior feeding vessel (arrow). Note parasitized arteries (arrowheads) from left renal artery to periaortic nodal masses seen on CT. (C) Embolization of entire left kidney with 1:1 lipiodol and ethanol. (D) Embolization of parasitized artery to periaortic nodal masses. (E) Postembolization angiogram demonstrates lack of forward flow in left renal artery (arrow).

fluoroscopy.[15–17] The abdominal aorta may be difficult to opacify adequately with CO_2, however, and selective renal CO_2 arteriography often has excellent results.

AML is most commonly fed by a single artery but can otherwise appear identical to RCC with hypervascularity and delayed contrast staining (Fig. 1B). After renal arteriography, the feeding vessel can be selectively catheterized and embolized with a 4F catheter or using a coaxial microcatheter system. The material used in the figures was a 1:1 mixture of Ethiodol and ethanol. This also allows adequate visualization of material flow (Fig. 1C). The small feeding vessels usually do not allow for balloon occlusion, and therefore 100% ethanol is uncommonly used for AML. The flow should be continuously monitored during injection until there is near stationary flow of the distal vessel. A 5-minute delay following embolization allows time for coagulation. The flow is then reassessed via selective angiography (Fig. 1D). Care must be taken not to inject the contrast aggressively, which can cause material migration into nontarget vessels. After adequate flow occlusion the catheter can be withdrawn and a renal arteriogram again performed to evaluate for any further tumor staining from smaller feeding arteries not previously appreciated.

In RCC, embolization can be performed to control hemorrhage, presurgical hemostasis, or for unresectable disease (Fig. 2A). On occasion, we are consulted for embolization of bilateral RCC prior to nephron-sparing surgery. Subselective embolization with coaxial systems can be very helpful in these situations. On the initial angiogram, close attention should be given to the aorta and renal vasculature because parasitized vessels of the adrenal, gonadal, and mesenteric arteries are common (Fig. 2B). Arteriovenous fistulas (AVFs) are also occasionally found in RCC and may preclude treatment with small particles; therefore, meticulous inspection is necessary to visualize early draining veins. Several articles describe embolization of RCC with varying concentrations of Gelfoam, Ethiodol, and ethanol, but ethanol has emerged as the predominant ingredient in recent reports.[3,18,19] At our institution, we use the same concentration of 1:1 ethanol to Ethiodol for presurgical RCC embolization as used in AML embolization (Fig. 2C,D). If performing embolization with 100% ethanol, proximal balloon occlusion should be performed to prevent reflux of the radiolucent alcohol, which will also necessitate a 7F sheath to pass the balloon through the access site. The amount of alcohol needed to denature the area downstream can be determined by inflation of the occlusion balloon in the target vessel and measured injection of contrast distally until there is complete opacification of the arterial tree. The balloon should be deflated for a few seconds to allow blood to fill the vessel, which will aid in coagulation during embolization.[20] The adrenal artery should not be embolized because this could cause hypertensive crisis or delayed adrenal dysfunction. The ethanol can be injected either through the lumen of the occlusion balloon catheter or from a coaxial system. After infusion the balloon should be left inflated for 10 minutes and then slowly deflated to prevent turbulent flow and retrograde migration of the embolization material. If AVFs are present, coils can be deployed proximally. Newer retrievable coils may be safer in these cases where migration would cause pulmonary embolus. The size of the coils should be slightly larger than the feeding vessel to prevent distal migration. Again, a delay is given prior to angiography to allow coagulation regardless of the material (Fig. 2E).

Immediately following the procedure, patients occasionally complain of back or flank pain. We have noted a decrease in pain when alcohol is used because there is thought to be obliteration of the nerves or vessels to the nerves. Intravenous sedation and pretreatment with ketorolac tromethamine and ondansetron can also reduce postembolization syndrome, which occurs in $\sim$10% of cases.[14] We admit patients not going to the operating room for 24-hour observation. There have been case reports of transient hypertension after renal embolization necessitating medical treatment.[19] We have not had that experience. Most patients have little pain if alcohol is used in the embolization and are ambulatory within hours after the procedure.

After embolization of AML, follow-up imaging is recommended for several reasons: Contrast-enhanced CT can determine if the entire tumor was embolized, delineate change in tumor size, and demonstrate evidence of adjacent renal infarction (Fig. 1E). Although several studies have shown a low incidence of recurrence of isolated AMLs, patients with TS have a significant risk of regrowth after embolization. In the two largest studies of long-term follow-up after AML embolization, only TS patients had recurrences, and the time to recurrence varied from 1 month to 8 years.[8,21,22] A postprocedure CT within 2 months would likely be prudent; but there are no current recommendations for further follow-up. For patients that have nephron-sparing resection of embolized isolated RCC, interval follow-up contrast-enhanced CT as per the protocol for partial nephrectomy is considered adequate. Current recommendations for follow-up of VHL-associated RCC suggest yearly CT is most sensitive for recurrence, and that MR imaging and US may not detect smaller lesions mimicking cysts.[23,24]

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